

IN THE CLAIMS

1. (Currently Amended) A method for treating ~~a thrombotic~~ an atherosclerotic cardiovascular disease in a mammal, said method comprising:

administering to said mammal at a site susceptible to a thrombus a therapeutically effective amount of a pharmaceutical composition comprising a ~~[[viral]]~~ gutless adenovirus vector,

wherein said ~~[[viral]]~~ gutless adenovirus vector comprises a nucleotide sequence encoding human thrombomodulin having an amino acid sequence recited in SEQ ID NO:2 or its variant, ~~[[and]]~~ a regulatory element operably linked to said nucleotide sequence, and a stuffer sequence comprises a HPRT intron sequence, ~~wherein said human thrombomodulin has an amino acid sequence recited in SEQ ID NO:2~~ and wherein said human thrombomodulin or its variant is expressed in said mammal.

2. (Original) The method of Claim 1, wherein said pharmaceutical composition further comprises a pharmaceutically acceptable carrier.

3-4. (Canceled)

5. (Currently Amended) The method of Claim ~~[[4]]~~ 1, wherein said gutless adenovirus vector further comprises ~~is produced using a shuttle vector comprising the~~ nucleotide sequence recited in SEQ ID NO: 4.

6. (Currently Amended) The method of Claim 1, wherein said ~~nucleotide sequence encoding human thrombomodulin or its variant is operably linked to~~ promoter is a constitutive promoter.

7. (Currently Amended) The method of Claim 1, wherein said ~~nucleotide sequence encoding human thrombomodulin or its variant is operably linked to~~ regulatory element is a tissue-specific promoter.

8. (Original) The method of Claim 1, wherein said nucleotide sequence encoding human thrombomodulin or its variant is under the control of a regulatable expression system.

9. (Canceled)

10. (Withdrawn) The method of Claim 1, wherein said viral vector is an adeno-associated virus.

11. (Withdrawn) The method of Claim 1, wherein said viral vector is a retrovirus.

12. (Withdrawn) The method of Claim 1, wherein said viral vector is a lentivirus.

13. (Withdrawn) The method of Claim 12, wherein said lentivirus is a human immunodeficiency virus.

14. (Withdrawn) The method of Claim 1, wherein said viral vector is a herpes virus.

15. (Original) The method of Claim 1, wherein said pharmaceutical composition is administered to said mammal intravascularly, subcutaneously, or intramuscularly.

16. (Withdrawn) A method for treating a thrombotic disease in a mammal, said method comprising:

administering to said mammal a therapeutically effective amount of a pharmaceutical composition comprising a non-viral vector, wherein said non-viral vector comprises a nucleotide sequence encoding human thrombomodulin or its variant, and wherein said human thrombomodulin has an amino acid sequence recited in SEQ ID NO:2.

17. (Withdrawn) The method of Claim 16, wherein said pharmaceutical composition further comprises a pharmaceutically acceptable carrier.

18. (Withdrawn) The method of Claim 16, wherein said non-viral vector is a liposome.

19. (Withdrawn) The method of Claim 16, wherein said non-viral vector is a naked DNA molecule.

20. (Withdrawn) The method of Claim 16, wherein the nucleotide sequence encoding human thrombomodulin or its variant is operably linked to a constitutive promoter.

21. (Withdrawn) The method of Claim 16, wherein the nucleotide sequence encoding human thrombomodulin or its variant is operably linked to a tissue-specific promoter.

22. (Withdrawn) The method of Claim 16, wherein the nucleotide sequence encoding human thrombomodulin or its variant is under the control of a regulatable expression system.

23. (Withdrawn) The method of Claim 16, wherein said thrombotic disease is atherosclerotic cardiovascular disease, pulmonary hypertension, acute inflammatory diseases, end-stage renal failure disease, or Alzheimer disease.

24. (Withdrawn) A method for treating a thrombotic disease in a mammal, said method comprising:

administering to said mammal a therapeutically effective amount of thrombomodulin-producing cells,

wherein said thrombomodulin-producing cells are generated by introducing a polynucleotide encoding a human thrombomodulin or its variant into a cultured cell, and wherein said human thrombomodulin has an amino acids sequence recited in SEQ ID NO:2.

25. (Withdrawn) The method of Claim 24, wherein said culture cell is human umbilical vein endothelium cell (HUVEC).

26. (Withdrawn) The method of Claim 24, wherein said polynucleotide encoding a human thrombomodulin or its variant is introduced into said cultured cell by a viral vector.

27. (Withdrawn) The method of Claim 24, wherein said polynucleotide encoding a human thrombomodulin or its variant is introduced into said cultured cell by a non-viral vector.

28. (Withdrawn) The method of Claim 24, wherein said polynucleotide encoding a human thrombomodulin or its variant is introduced into said cultured cell by calcium phosphate precipitation.

29. (Withdrawn) The method of Claim 24, wherein said polynucleotide encoding a human thrombomodulin or its variant is introduced into said cultured cell by electroporation.

30. (New) A method for treating an atherosclerotic cardiovascular disease in a mammal, said method comprising:

administering to said mammal at a site susceptible to a thrombus a therapeutically effective amount of a pharmaceutical composition comprising a gutless adenovirus vector,

wherein said gutless adenovirus vector comprises a nucleotide sequence encoding human thrombomodulin having an amino acid sequence recited in SEQ ID NO:2 or its variant, a promoter operably linked to said nucleotide sequence, and the nucleotide sequence recited in SEQ ID NO: 4, and wherein said human thrombomodulin or its variant is expressed in said mammal.